

10/522043  
Amendments to the Claims PTO1 Rec'd PCT/PTO 19 JAN 2005

1. (currently amended) An isolated nucleic acid molecule which encodes a polypeptide, or sequence variant thereof, wherein said polypeptide is a fragment of the polypeptide sequence represented in SEQ ID NO: 8 or 9 Figure 1a or 1b, wherein the fragment is which fragment is selected from the group consisting of:
  - i) a polypeptide fragment consisting of amino acid residues from about residue 128-224 of the amino acid sequence presented in SEQ ID NO: 8 or 9 Figure 1a or 1b;
  - ii) or a polypeptide fragment consisting of amino acid residues from about residue 128-224 of the amino acid sequence presented in SEQ ID NO: 8 or 9 Figure 1a or 1b wherein said sequence has been modified by addition, deletion or substitution of at least one amino acid residue, wherein the polypeptide inhibits the apoptotic activity of p53; and
  - ~~a polypeptide as defined in (i) and (ii) wherein said polypeptide substantially retains the biological activity of the polypeptide represented in Figure 1a or 1b.~~
2. (currently amended) A The nucleic acid molecule according to Claim 1, wherein said molecule encodes a fragment consisting of amino acid residues from about residue 128-224 of the sequence represented in SEQ ID NO: 8 Figure 1a.
3. (currently amended) A The nucleic acid molecule according to Claim 2, wherein said molecule is isolated from a human.
4. (currently amended) A The nucleic acid molecule according to Claim 1, ~~or 2~~ wherein said molecule encodes a fragment consisting of amino acid residues from about residue 128-224 of the sequence represented in SEQ ID NO: 9 Figure 1b.
5. (currently amended) A The nucleic acid molecule according to Claim 4, wherein said molecule is isolated from a nematode.

6. (currently amended) A The nucleic acid molecule according to Claim 5, wherein said nematode is of the genus *Caenorhabditis spp.*
7. (canceled)
8. (currently amended) A The nucleic acid molecule according to Claim 1, any of Claims 1-7 wherein said nucleic acid molecule is a cDNA or genomic DNA.
9. (canceled)
10. (currently amended) A polypeptide fragment or sequence variant thereof, encoded by a the nucleic acid molecule according to Claim 1 any of Claims 1-9.
11. (currently amended) A vector comprising a the nucleic acid according to Claim 1 any of Claims 1-9.
12. (currently amended) A The vector according to Claim 11, wherein said vector is an expression vector.
13. (currently amended) A cell transformed or transfected with a the nucleic acid molecule according to Claim 1 any of Claims 1-9 or a vector according to Claim 11 or 12.
14. (currently amended) A pharmaceutical composition comprising the nucleic acid according to Claim 1 any of Claims 1-9 for use as a pharmaceutical.
15. (currently amended) A pharmaceutical composition comprising the polypeptide according to Claim 10 for use as a pharmaceutical.
16. (canceled)

17. (currently amended) A transgenic non-human animal comprising a the nucleic acid molecule according to Claim 1 any of Claims 1-9.
18. (canceled)
19. (currently amended) A screening method to identify agents which inhibit the binding of a polypeptide, or fragment thereof, to p53 comprising:
  - i)- forming a preparation comprising
    - e)- a the polypeptide of Claim 10 according to the invention; and
    - d)- a p53 polypeptide, or a fragment thereof consisting of the binding site(s) for the polypeptide of Claim 10 in (a);
  - ii)- providing at least one agent to be tested; and
  - iii)- determining the activity of the agent with respect to the binding of the polypeptide of Claim 10 in (a) to the p53 polypeptide, or a fragment thereof consisting of the binding site(s) for the polypeptide of Claim 10 in (b).
20. (currently amended) A The method according to Claim 19, wherein said agent is a polypeptide or a peptide.
21. (canceled)
22. (currently amended) A The method according to Claim 20, wherein said polypeptide is an antibody or binding part thereof.
23. (currently amended) A The method according to Claim 22, wherein said antibody is a monoclonal antibody.
24. (currently amended) A The method according to Claim 22, Claim 22 or 23 wherein said fragment is an Fab fragment.

25. (currently amended) A The method according to Claim 24, wherein said Fab fragment is selected from the group consisting of: an F(ab')<sub>2</sub> fragment, an Fab fragment, an Fv fragment, and Fd fragments; and or CDR3 regions.
26. (currently amended) A The method according to Claim 23, any of Claims 23-25 wherein said antibody is  $\alpha$ -humanised.
27. (currently amended) A The method according to Claim 23, any of Claims 23-25 wherein said antibody is a chimeric antibody.
28. (currently amended) An isolated nucleic acid molecule, wherein said molecule is isolated from a nematode worm ~~which nucleic acid molecule~~ and hybridises to the a nucleic acid sequence shown in SEQ ID NO: 9 as represented by Fig 1b, wherein said nucleic acid molecule encodes an inhibitor of p53 and inhibits the apoptotic activity of p53.
29. (currently amended) A The nucleic acid molecule according to Claim 28, wherein said molecule hybridises under stringent hybridisation conditions.
30. (canceled)
31. (currently amended) An isolated polypeptide comprising the amino acid sequence as represented in SEQ ID NO: 9Figure 2b or a variant polypeptide which polypeptide is modified by addition, deletion or substitution of at least one amino acid residue and is an inhibitor of p53.
32. (currently amended) A method of treatment of an animal, comprising administering an effective amount of a the polypeptide according to Claim 10, wherein said effective amount induces the apoptotic apoptotic activity of p53.

33. (currently amended) A method of treatment of an animal comprising administering an effective amount of a nucleic acid molecule according to Claim 1, any of Claims 1-9 or a vector according to Claim 11 or 12 wherein said effective amount induces the apoptotic apoptotic activity of p53.

34. (currently amended) A The method according to Claim 32, Claim 32 or 33 wherein said treatment is of cancer.

35. (currently amended) The polypeptide of Claim 10, wherein the polypeptide is a peptide comprising an amino acid sequence selected from the group consisting of: DGPEETD (SEQ ID NO: 2); GPEETD (SEQ ID NO: 2); TTLSDG (SEQ ID NO: 3); AEFGDE (amino acids 294-299 of SEQ ID NO: 8); or PRNYFG (SEQ ID NO: 4).

36. (currently amended) A The peptide according to Claim 35, wherein the length of said peptide is at least 6 amino acid residues.

37. (currently amended) A The peptide according to Claim 35, wherein the length of said peptide is selected from the group consisting of: is at least 7, amino acid residues; 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 amino acid residues.

38. (currently amended) A The peptide according to Claim 35, wherein the length of said peptide is at least 20, amino acid residues; 30; 40; 50; 60; 70; 80; 90; or 100 amino acid residues.

39. (currently amended) A The peptide according to Claim 35, wherein the peptide consists of the consisting of an amino acid sequence selected from the group consisting of: DGPEETD (SEQ ID NO: 2); GPEETD (SEQ ID NO: 1); TTLSDG (SEQ ID NO: 3); AEFGDE (amino acids 294-299 of SEQ ID NO: 8); or PRNYFG (SEQ ID NO: 4).

40. (canceled)

41. (currently amended) A The peptide according to Claim 3540, wherein the peptide further comprises said plurality of arginine residues is at least 2, 3, 4, 5, 6, 7, 8, 9, or 10 arginine residues in length.

42. (canceled)

43. (currently amended) A pharmaceutical composition comprising the peptide of Claim 35 a peptide selected from the group consisting of: DGPEETD; GPEETD; TTLSDG; AEFGDE; or PRNYFG.

44. (currently amended) A The pharmaceutical composition according to Claim 43, wherein said composition further includes a carrier, diluent or excipient.

45. (currently amended) A The pharmaceutical composition of Claim 35 further comprising at least one peptide according any of Claims 35-42 and at least one anti-cancer agent.

46. (currently amended) A The pharmaceutical composition according to Claim 45 wherein said anticancer agent is selected from the group consisting of: cisplatin; carboplatin; cyclophosphamide; melphalan; carmustine; methotrexate; 5-fluorouracil; cytarabine; mercaptopurine; daunorubicin; doxorubicin; epirubicin; vinblastine; vincristine; dactinomycin; mitomycin C; taxol; L-asparaginase; G-CSF; etoposide; colchicine; derferroxamine mesylate; or and camptothecin.

47. (canceled)

48. (canceled)

49. (currently amended) A complex comprising a the peptide according to Claim 35 any of Claims 35-42 and an antibody, or binding part thereof.

50. (currently amended) A The complex according to Claim 49, wherein said antibody or binding part is a cell specific antibody.

51. (currently amended) A The complex according to Claim 49 or 50 wherein said antibody is a cancer cell specific antibody.

52. (currently amended) A method of treatment of an animal that, preferably a human, wherein said animal would benefit from the induction of apoptosis, comprising administering an effective amount of a the peptide of Claim 35 to the animal according to any of Claims 35-41.

53. (canceled)

54. (currently amended) A The method according to Claim 52 or 53 wherein said treatment is cancer treatment.